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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KIM, YOUNG J	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 08/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/788,529	ROTHBERG ET AL.	
	Examiner	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6,8,9,12-17,23-29 and 63-74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6,8,9,12-17,23-29 and 63-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/12/05 & 12/5/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 6, 8, 9, 12-17, 23-29, and 63-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chee et al. (2003/0108867 A1, published June 12, 2003, priority April 20, 1999; IDS ref# 166[1]) in view of Krull et al. (WO 98/58079, published December 23, 1998; IDS reference B90[2]).

Chee et al. disclose a method of using a substrate (and apparatus comprising the substrate) for pyrosequencing a nucleic acid template, wherein the substrate is comprised of a bundle of plurality of fused, optical fibers which are "etched" such that small wells or depressions are formed at the end of the fibers (or cavitated) (Figure 1A-D, [0109], and [0112]). The cavitated optical fibers also comprise microspheres immobilized with capture probes ([0052]) and immobilized pyrosequencing reagents ([0057]).

Chee et al. disclose that the nucleic acids or DNAs ([0093]; claim limitation 87 and 101) are immobilized to the microspheres by linkers or covalently ([0015] and [0057]).

The substrate of Chee et al. is disclosed being able to have a wide range of nucleic acids, ranging from 10^2 to 10^9 ([0104]; claim limitation 64-66) as well as being chemically functionalized for photolithography ([0111]-[0114]).

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[1] IDS received on May 12, 2005.
[2] IDS received on December 5, 2005.

The immobilized pyrosequencing reagents (on the micrspheres, [0057]) are disclosed as being luciferase, sulfurylase, or apyrase ([0040]).

Although Chee et al. do not explicitly disclose that the imaging of the sequencing reaction is done through CCD (charge coupled device), such is implicit by the disclosure of the specification, wherein the artisans image the incorporated nucleotide in their fiber optic substrate ([0192]).

Chee et al. do not *explicitly disclose* the diameter of the individual optical fiber nor the cavitated fiber optic wafer having a depth between 0.5 mm and 5.0 mm.

Chee et al. do not *explicitly disclose* various separation distance between the nucleic acids that are immobilized on the substrate or microspheres.

Chee et al. do not explicitly disclose that a polished end of a fiber optic wafer is optically linked to a second fiber optic fiber.

Krull et al. disclose a fiber optic array, said array comprising an optical substrate such as an optical wafer or an optical fiber (page 13, lines 16-19), wherein nucleic acids are immobilized thereto.

Krull et al. disclose a detector for optical detection of the labels (page 11, line 30 through page 12, line 4; Figure 4(c)).

Krull et al. disclose a sensor fiber optic bundles having the length of (page 43, line 7-10; or a wafer having 1 cm depth), wherein one of the ends of each optical fiber is polished (page 43, line 10). The sensor fiber optic bundles has immobilized there to nucleic acid probes (page 51, lines 25-31), wherein said sensor fiber has optically coupled thereto, a delivery fiber which carries the excitation light (page 67, lines 12-16), delivering the light through the sensing fiber (page 67, lines 16-18) as well as carrying the excitation of the labels back to the detection module (page 68, lines 4-6).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Chee et al. with the teachings of Krull et al. for the following reasons.

Chee et al. already disclose a substrate formed from fused optical fibers (along their lengths), wherein the optical fibers are cavitated, having immobilized thereto beads comprising nucleic acids or pyrophosphate sequencing reagents therein (discussed above). The difference between the teachings of Chee et al. and of the claimed substrate (and apparatus comprising the substrate) is in that the substrate has a depth ranging from 0.5mm to 5mm (producing a wafer configuration).

However, Krull et al. disclose a sensor probe made from fused optical fibers having limited length (of 1 cm), wherein the light source (delivery fiber) is optically connected to the sensor probe so as to achieve detection. Krull et al. are clearly in discussing that optical coupling of the two ends of the optical fibers are efficient, with "no greater than 2% loss" in optical transmission (page 67, lines 18-19).

Additionally, it is asserted that the length of the fiber optic bundle does not materially affect the ability of the substrate in transmitting the signals produced from a ligand binding assays. This is evident in Applicants' claim 89, which requires that the ends of the shortened fiber optic bundles (of the wafer) be attached to second optical fiber bundles to be able to transmit the data across to the imaging device. The net effect, therefore, requires a long bundle of fiber optic fibers attached to an imaging device, resulting in the fiber optic array disclosed by Chee et al.

This is evident in Applicants' own disclosure, which requires that the ends of the shortened fiber optic bundles (of the wafer) ***be attached*** to second fiber bundles to be able to ***transmit the data across*** to the imaging device:

"In some embodiments two fiber optic bundles are used: a first bundle is attached directly to the CCD sensor (the fiber bundle or connector or solid support) and the second bundle is used in the perfusion chamber substrate (the wafer or substrate). In this case the ***two are placed in direct contact***, optionally with the use of optical coupling fluid, ***in order to image the reaction center on to the CCD sensor***" [0156].

Hence, for the method to work, the identical structure to that of Chee et al. must be produced, that is, a long bundle of optical fibers attached to an imaging device.

Therefore, at best, the shortened length of the fiber optic bundle with any depth only results in the portability of the claimed substrates."

> "The desired number of optical fibers are initially fused into a bundle, the terminus of which is cut and polished so as to form a "wafer" of the required thickness...[t]he resulting optical fiber wafers possess similar handling properties to that of a glass plane of glass" ([0155], instant specification).

However, MPEP 2144.04(V), in discussing portability, states:

> "In *in re Lindberg*, 194 F.2d 732, 93 USPQ 23 (CCPA 1952) (Fact that a claimed device is portable or movable ***is not sufficient by itself to patentably distinguish over an otherwise old device unless there are new or unexpected results***)"

In view of this decision, the claimed method employing an array formed from fused fiber optic bundles, the array of which is an the form of a wafer having a recited range of depth for the sole purpose of portability, ***would not*** patentably distinguish it from a method involving an "old device" (that is the optical array of Chee et al.), because there are ***no*** new or unexpected results produced (from making the device portable).

Coupled with the teachings of Krull et al. who explicitly state that the form of a long optical fiber or an optical wafer format could be used as well as employing optical coupling of two optical

fibers to transmit light to the detector, one of ordinary skill in the art at the time the invention was made would have had a clearly expectation of success at producing the claimed invention (rendering claims 56, 58, 84, 85, 88, and 89 obvious over the cited references.

Since Chee et al. disclose that because beads of 200 um or less (with beads of 200 nm possible) can be used, and very small fibers are known, it is possible to have as many as 40,000 or more (in some instances, 1 million) different elements (e.g., fibers and beads) in a 1mm^2 fiber optic bundle, with densities of greater than 25,000,000 individual beads and fibers per 0.5 cm^2 obtainable [0105]. Moreover, one of ordinary skill in the art would have been able to determine the proper separation distance between the nucleic acids so as to achieve maximum density without interference based on such a guidance.

For the above reasons, the invention as claimed is *prima facie* obvious over the cited references.

Conclusion

No claims are allowed.

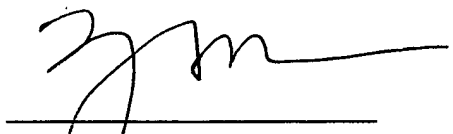
Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is on flex-time schedule and can best be reached from 8:30 a.m. to 4:30 p.m (M-W and F). The Examiner can also be reached via e-mail to Young.Kim@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official

Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.



Young J. Kim
Primary Examiner
Art Unit 1637
8/7/2006

YJK